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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,803	11/14/2005	Giuseppe Arpaia	279737US0PCT	1463
22850	7590	02/03/2010	EXAMINER	
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P. 1940 DUKE STREET ALEXANDRIA, VA 22314			XU, XIAOYUN	
			ART UNIT	PAPER NUMBER
			1797	
			NOTIFICATION DATE	DELIVERY MODE
			02/03/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/556,803	Applicant(s) ARPAIA ET AL.	
	Examiner ROBERT XU	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed on 01/21/2010 has been entered and fully considered. Claims 23 and 24 are canceled. Claims 15-17 are pending, of which Claim 15 is amended.

Response to Amendment

2. In response to amendment, the examiner maintains rejection over the prior art established in the previous Office action.

Claim Objections

3. Claim 15 is objected to because of the following informalities: Claim 15 recites "100 g/ml". The correct word should be "100 µg/ml", because only 100 µg/ml of Pluronic F68 (Poloxamer 188) is supported by the specification (see page 11, line 20). Based on Applicant's remark, 100 g/ml must be a type error. Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. **Claims 15 -17** are rejected under 35 U.S.C. 103(a) as being unpatentable over Katakam et al. (Pharmaceutical Development and Technology, 1997) (Katakam) in view of Wu (Journal of Endocrinology, 1993).

In regard to Claim 15, Katakam teaches the use of Poloxamer polymer to stabilize recombinant human growth hormone (rhGH) against various processing stress (see title). The method comprises:

mixing the protein sample (rhGH) by adding a Poloxamer 188 (Pluronic F68) to the sample (see page 144, left col. 3rd paragraph, Table 1);
performing chromatography (size exclusion column- HPLC) on the protein sample (see page 145, right col. 1st paragraph); and
the quantity of the total protein is determined by UV absorbance of the eluted protein solution (see page 145, right col. 1st paragraph and Figure 1-2).

Katakam tests various concentrations of Poloxamer 188 (Pluronic 68) in the range from 0.001% (below cmc) to 0.2% (above cmc) (see Table 1). The concentration of 100 µg/ml is equivalent to 0.01%. Katakam's teaching meets the recited limitation.

Katakam does not specifically teach using data from calibration with a standard to calculate the quantity of the protein. However, using data from calibration with a standard to calculate the quantity of the protein is well known in the art. At time of the invention, it would have been obvious for a person of ordinary skill in the art to use data from calibration with a standard to calculate the quantity of the protein.

Katakam does not teach FSH. Wu teaches that FSH from bovine pituitary glands is isolated by size exclusion (gel filtration) chromatography (see abstract). Since Katakam demonstrates that Poloxamer reduces aggregation of HGH, it would have been obvious to one of ordinary skill in the art to apply the same method on other proteins. From particular to general is how science and engineering developed.

In regard to Claim 16, simple dilution of protein sample to a level acceptable for the chromatographic system is well-known in the art.

In regard to Claim 17, Katakam teach using size-exclusion chromatography (SEC) to quantify protein (see page 145, right col. 1st paragraph).

Response to Arguments

6. Applicant's arguments filed 01/21/2010 have been fully considered but they are not persuasive.

Applicant submits that the concentration of Poloxamer 188 recited in Claim 15 (0.01%) is much closer to the "non-working" concentration of Poloxamer 188 (0.0055%), than to the "working" one (0.2%) according to Katakam et al. Therefore, the skilled person had no motivation to try Poloxamer 188 as stabilizer at a concentration which is less than double the CMC, knowing in addition that Poloxamer 188 works well at much higher concentrations, i.e. concentration over 36 times the cmc.

Examiner respectfully disagrees. 0.2% of Poloxamer in Table 1 is one data point in Katakam's tests in a range from 0.001% to 0.2%. Katakam teaches that: "since surfactants adsorb preferentially at the air/water interface, they are believed to minimize

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aggregation by reducing the adsorption of protein at interfaces. As a surfactant forms a complete monolayer at the surface at its critical micelle concentration (cmc), the protection is expected to be linked to the cmc value" (see page 146, left col. 1st paragraph). Katakam further gives examples: (1) "at a concentration of 0.2%, which was higher than the cmc of all poloxamers, the aggregation of rhGH was prevented by all poloxamers as evidenced by the lack of absorbance at 400nm as well as SEC-HPLC assay"; (2) "Below and at cmc, only Poloxamer 407 was found to be effective" (see page 146, left col. 1st paragraph). Thus, ordinary skill in the art would have learned that cmc is a critical concentration that needs to be exceeded in order to form a complete monolayer at the surface of micelle. The 0.01% of Poloxamer 188 is twice of cmc (0.0055%) needed for the surfactant to form a complete monolayer on the surface of micelle as taught by Katakam. Therefore, at the time of the invention it would have been obvious for a routineer to try 0.01% of Poloxamer 188 first, because it would save money and cause no harm to protein by trying low concentration of surfactant first.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1/28/2010

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

RX